



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket No: SALK1720-6

In re patent application of

MATHEWS, LAWRENCE S. et al.

Serial No. 09/742,684

Filed: December 19, 2000

For: CLONING AND RECOMBINANT PRODUCTION OF RECEPTOR(S) OF
THE ACTIVIN/TGF-BETA SUPERFAMILY

STATEMENT TO SUPPORT FILING AND SUBMISSION IN
ACCORDANCE WITH 37 C.F.R. §§ 1.821-1.825

RECEIVED

Assistant Commissioner for Patents
Washington, D.C. 20231
Box SEQUENCE

MAY 02 2003

TECH CENTER 1600/2900

Sir:

In connection with a Sequence Listing submitted concurrently herewith, the undersigned hereby states that:

1. the submission, filed herewith in accordance with 37 C.F.R. § 1.821(g), does not include new matter;

2. the content of the attached paper copy and the attached computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.821(c) and (e), respectively, are the same.

Respectfully submitted,

David M. Narkunas
Reg. No. 53,370

Date

April 22, 2003

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1500A Lafayette Road, #262
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800-318-3021



1

SEQUENCE LISTING

<110> MATHEWS, LAWRENCE S.
VALE JR., WYLIE W.
TSUCHIDA, KUNIHIRO

<120> CLONING AND RECOMBINANT PRODUCTION OF RECEPTOR(S) OF
THE ACTIVIN/TGF-BETA SUPERFAMILY

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<220>
<221> MOD_RES

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<222> (3)
<223> Ile or Val

<220>
<221> MOD_RES
<222> (4)
<223> Lys or Arg

<220>
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<222> (6)
<223> Thr or Met

<400> 10
Xaa Pro Xaa Xaa Trp Xaa
    1           5

<210> 11
<211> 1602
<212> DNA
<213> Rattus sp.

<220>
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<222> (72)...(1550)

<400> 11
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gcgggggtggc c atg acc cca gcg cgc tcc gca ctg agc ctg gcc ctc 110
Met Thr Pro Ala Arg Arg Ser Ala Leu Ser Leu Ala Leu
    1           5           10

ctg ctg gtg gca ctg gcc tcc gac ctt gcg gca gga ctg aag tgt gtg 158
Leu Leu Val Ala Leu Ala Ser Asp Leu Ala Gly Leu Lys Cys Val
    15          20           25

tgt ctt ttg tgt gat tcc tca aac ttt acc tgc caa acc gaa gga gca 206
Cys Leu Leu Cys Asp Ser Ser Asn Phe Thr Cys Gln Thr Glu Gly Ala
    30          35           40           45

tgc tgg gcc tct gtc atg cta acc aac ggg aaa gaa cag gtg agc aaa 254
Cys Trp Ala Ser Val Met Leu Thr Asn Gly Lys Glu Gln Val Ser Lys
    50           55           60

tcg tgc gtg tcc ctc ccg gaa cta aat gct cag gtc ttc tgt cac agt 302
Ser Cys Val Ser Leu Pro Glu Leu Asn Ala Gln Val Phe Cys His Ser
    65           70           75

tcc aac aac gtg acc aag acc gaa tgt tgc ttc aca gac ttc tgc aac 350
Ser Asn Asn Val Thr Lys Thr Glu Cys Cys Phe Thr Asp Phe Cys Asn
    80           85           90

aac atc act cag cac ctt ccc aca gca tct cca gat gcc cct aga ctt 398
Asn Ile Thr Gln His Leu Pro Thr Ala Ser Pro Asp Ala Pro Arg Leu
    95          100          105

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ggc ccc aca gag ctg aca gtt gtt atc act gta cct gtt tgc ctc ctg Gly Pro Thr Glu Leu Thr Val Val Ile Thr Val Pro Val Cys Leu Leu 110 115 120 125	446
tcc atc gca gcc atg cta acg ata tgg gcc tgc cag gac cgc cag tgc Ser Ile Ala Ala Met Leu Thr Ile Trp Ala Cys Gln Asp Arg Gln Cys 130 135 140	494
aca tac agg aag acc aag aga cac aat gtg gag gaa cca ctg gca gag Thr Tyr Arg Lys Thr Lys Arg His Asn Val Glu Glu Pro Leu Ala Glu 145 150 155	542
tac agc ctt gtc aat gct gga aaa acc ctc aaa gat ctg att tat gat Tyr Ser Leu Val Asn Ala Gly Lys Thr Leu Lys Asp Leu Ile Tyr Asp 160 165 170	590
gcc act gcc tcg ggc tca gga tct ggc ccg cct ctt ttg gtt caa aga Ala Thr Ala Ser Gly Ser Gly Pro Pro Leu Leu Val Gln Arg 175 180 185	638
acc atc gca agg aca att gta ctt caa gaa atc gta gga aaa ggt cgg Thr Ile Ala Arg Thr Ile Val Leu Gln Glu Ile Val Gly Lys Gly Arg 190 195 200 205	686
ttt ggg gaa gtg tgg cac gga aga tgg tgt gga gaa gat gtg gct gtg Phe Gly Glu Val Trp His Gly Arg Trp Cys Gly Glu Asp Val Ala Val 210 215 220	734
aaa ata ttc tcc tcc aga gat gag aga tct tgg ttc cgt gag gca gaa Lys Ile Phe Ser Ser Arg Asp Glu Arg Ser Trp Phe Arg Glu Ala Glu 225 230 235	782
att tat cag acg gta atg ctg aga cat gag aat att ctc ggt ttc atc Ile Tyr Gln Thr Val Met Leu Arg His Glu Asn Ile Leu Gly Phe Ile 240 245 250	830
gcg gcc gac aac aaa gat aat gga acc tgg act cag ctt tgg ctt gtg Ala Ala Asp Asn Lys Asp Asn Gly Thr Trp Thr Gln Leu Trp Leu Val 255 260 265	878
tca gag tat cac gag cag ggc tcc tta tat gac tat ttg aat aga aac Ser Glu Tyr His Glu Gln Gly Ser Leu Tyr Asp Tyr Leu Asn Arg Asn 270 275 280 285	926
ata gtg acc gtg gct gga atg gtc aag ttg gcg ctt tca ata gcg agt Ile Val Thr Val Ala Gly Met Val Lys Leu Ala Leu Ser Ile Ala Ser 290 295 300	974
ggt ctg gct cac cta cac atg gag atc gtg ggc act caa ggt aag cct Gly Leu Ala His Leu His Met Glu Ile Val Gly Thr Gln Gly Lys Pro 305 310 315	1022
gct att gct cac cga gat ata aag tca aag aat atc tta gtc aaa aag Ala Ile Ala His Arg Asp Ile Lys Ser Lys Asn Ile Leu Val Lys Lys 320 325 330	1070

tgt gac act tgt gcc ata gct gac tta ggg ctg gct gtg aaa cat gat Cys Asp Thr Cys Ala Ile Ala Asp Leu Gly Leu Ala Val Lys His Asp 335 340 345	1118
tct atc atg aac act ata gat ata ccc cag aat cct aaa gtg gga acc Ser Ile Met Asn Thr Ile Asp Ile Pro Gln Asn Pro Lys Val Gly Thr 350 355 360 365	1166
aag agg tat atg gct ccc gaa atg ctt gat gat aca atg aac gtc aac Lys Arg Tyr Met Ala Pro Glu Met Leu Asp Asp Thr Met Asn Val Asn 370 375 380	1214
atc ttt gag tcc ttc aag cga gct gac atc tat tcg gtg ggg ctg gtt Ile Phe Glu Ser Phe Lys Arg Ala Asp Ile Tyr Ser Val Gly Leu Val 385 390 395	1262
tac tgg gaa ata gct cga agg tgt tca gtt gga gga ctt gtt gaa gag Tyr Trp Glu Ile Ala Arg Arg Cys Ser Val Gly Gly Leu Val Glu Glu 400 405 410	1310
tac cag ttg cct tat tat gac atg gtg cct tca gat cct tcc ata gag Tyr Gln Leu Pro Tyr Tyr Asp Met Val Pro Ser Asp Pro Ser Ile Glu 415 420 425	1358
gaa atg agg aag gtc gtt tgt gat cag aaa ctg cga cca aat ctc cca Glu Met Arg Lys Val Val Cys Asp Gln Lys Leu Arg Pro Asn Leu Pro 430 435 440 445	1406
aac cag tgg caa agc tgt gag gcg ctc cgg gtc atg gga aga ata atg Asn Gln Trp Gln Ser Cys Glu Ala Leu Arg Val Met Gly Arg Ile Met 450 455 460	1454
cgt gag tgc tgg tat gcc aac ggg gca gct cgc ctg acc gcc ctg cgc Arg Glu Cys Trp Tyr Ala Asn Gly Ala Ala Arg Leu Thr Ala Leu Arg 465 470 475	1502
gtg aag aag acc att tct cag ctg tgt gtc aag gaa gac tgt aag gcc Val Lys Lys Thr Ile Ser Gln Leu Cys Val Lys Glu Asp Cys Lys Ala 480 485 490	1550
taaggataaca ggccgacggga aagccctcac cactctcttt catgtctcct gc	1602
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Cys Asp Ser Ser Asn Phe Thr Cys Gln Thr Glu Gly Ala Cys Trp Ala 35 40 45	

Ser Val Met Leu Thr Asn Gly Lys Glu Gln Val Ser Lys Ser Cys Val
 50 55 60

Ser Leu Pro Glu Leu Asn Ala Gln Val Phe Cys His Ser Ser Asn Asn
 65 70 75 80

Val Thr Lys Thr Glu Cys Cys Phe Thr Asp Phe Cys Asn Asn Ile Thr
 85 90 95

Gln His Leu Pro Thr Ala Ser Pro Asp Ala Pro Arg Leu Gly Pro Thr
 100 105 110

Glu Leu Thr Val Val Ile Thr Val Pro Val Cys Leu Leu Ser Ile Ala
 115 120 125

Ala Met Leu Thr Ile Trp Ala Cys Gln Asp Arg Gln Cys Thr Tyr Arg
 130 135 140

Lys Thr Lys Arg His Asn Val Glu Glu Pro Leu Ala Glu Tyr Ser Leu
 145 150 155 160

Val Asn Ala Gly Lys Thr Leu Lys Asp Leu Ile Tyr Asp Ala Thr Ala
 165 170 175

Ser Gly Ser Gly Ser Gly Pro Pro Leu Leu Val Gln Arg Thr Ile Ala
 180 185 190

Arg Thr Ile Val Leu Gln Glu Ile Val Gly Lys Gly Arg Phe Gly Glu
 195 200 205

Val Trp His Gly Arg Trp Cys Gly Glu Asp Val Ala Val Lys Ile Phe
 210 215 220

Ser Ser Arg Asp Glu Arg Ser Trp Phe Arg Glu Ala Glu Ile Tyr Gln
 225 230 235 240

Thr Val Met Leu Arg His Glu Asn Ile Leu Gly Phe Ile Ala Ala Asp
 245 250 255

Asn Lys Asp Asn Gly Thr Trp Thr Gln Leu Trp Leu Val Ser Glu Tyr
 260 265 270

His Glu Gln Gly Ser Leu Tyr Asp Tyr Leu Asn Arg Asn Ile Val Thr
 275 280 285

Val Ala Gly Met Val Lys Leu Ala Leu Ser Ile Ala Ser Gly Leu Ala
 290 295 300

His Leu His Met Glu Ile Val Gly Thr Gln Gly Lys Pro Ala Ile Ala
 305 310 315 320

His Arg Asp Ile Lys Ser Lys Asn Ile Leu Val Lys Lys Cys Asp Thr
 325 330 335

Cys Ala Ile Ala Asp Leu Gly Leu Ala Val Lys His Asp Ser Ile Met
 340 345 350

Asn Thr Ile Asp Ile Pro Gln Asn Pro Lys Val Gly Thr Lys Arg Tyr
 355 360 365
 Met Ala Pro Glu Met Leu Asp Asp Thr Met Asn Val Asn Ile Phe Glu
 370 375 380
 Ser Phe Lys Arg Ala Asp Ile Tyr Ser Val Gly Leu Val Tyr Trp Glu
 385 390 395 400
 Ile Ala Arg Arg Cys Ser Val Gly Gly Leu Val Glu Glu Tyr Gln Leu
 405 410 415
 Pro Tyr Tyr Asp Met Val Pro Ser Asp Pro Ser Ile Glu Glu Met Arg
 420 425 430
 Lys Val Val Cys Asp Gln Lys Leu Arg Pro Asn Leu Pro Asn Gln Trp
 435 440 445
 Gln Ser Cys Glu Ala Leu Arg Val Met Gly Arg Ile Met Arg Glu Cys
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<210> 13
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

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<221> modified_base
<222> (11)
<223> a, t, c or g

<220>
<221> modified_base
<222> (14)
<223> a, t, c or g

<220>
<221> modified_base
<222> (17)
<223> a, t, c or g

<400> 13
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28

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<210> 14
<211> 35

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<212> DNA
<213> Artificial Sequence

<220>
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<222> (12)
<223> a, t, c or g

<220>
<221> modified_base
<222> (15)
<223> a, t, c or g

<220>
<221> modified_base
<222> (24)
<223> a, t, c or g

<220>
<221> modified_base
<222> (30)
<223> a, t, c or g

<220>
<221> modified_base
<222> (33)
<223> a, t, c or g

<400> 14
cgggatccyt cnggngccat rtanckyctn gtncc 35

<210> 15
<211> 2563
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (71)..(1609)

<220>
<221> modified_base
<222> (346)
<223> a, t, c or g

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cctcgggaaa atg gga gct gct gca aag ttg gcg ttc gcc gtc ttt ctt 109
Met Gly Ala Ala Ala Lys Leu Ala Phe Ala Val Phe Leu
          1           5            10

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tgt ctt ttc ttt aat gct aat tgg gaa aar gac aga acc aac cag act Cys Leu Phe Phe Asn Ala Asn Trp Glu Lys Asp Arg Thr Asn Gln Thr	30	35	40	45	205
ggt gtt gaa cct tgc tat ggt gat aaa gat aaa cgg cga cat tgt ttt Gly Val Glu Pro Cys Tyr Gly Asp Lys Asp Lys Arg Arg His Cys Phe	50	55	60		253
gct acc tgg aag aat att tct ggt tcc att gaa ata gtg aag caa ggt Ala Thr Trp Lys Asn Ile Ser Gly Ser Ile Glu Ile Val Lys Gln Gly	65	70	75		301
tgt tgg ctg gat gat atc aac tgc tat gac agg act gat tgt gtn gaa Cys Trp Leu Asp Asp Ile Asn Cys Tyr Asp Arg Thr Asp Cys Val Glu	80	85	90		349
aaa aaa gac agc cct gaa gtg tac ttt tgt tgc tgt gag ggc aat atg Lys Lys Asp Ser Pro Glu Val Tyr Phe Cys Cys Cys Glu Gly Asn Met	95	100	105		397
tgt aat gaa aag ttc tct tat ttt ccg gag atg gaa gtc aca cag ccc Cys Asn Glu Lys Phe Ser Tyr Phe Pro Glu Met Glu Val Thr Gln Pro	110	115	120	125	445
act tca aat cct gtt aca ccg aag cca ccc tat tac aac att ctg ctg Thr Ser Asn Pro Val Thr Pro Lys Pro Pro Tyr Tyr Asn Ile Leu Leu	130	135	140		493
tat tcc ttg gta cca cta atg tta att gca gga att gtc att tgt gca Tyr Ser Leu Val Pro Leu Met Leu Ile Ala Gly Ile Val Ile Cys Ala	145	150	155		541
ttt tgg gtg tac aga cat cac aag atg gcc tac cct cct gta ctt gtt Phe Trp Val Tyr Arg His His Lys Met Ala Tyr Pro Pro Val Leu Val	160	165	170		589
cct actcaa gac cca gga cca ccc cca cct tcc cca tta cta ggg ttg Pro Thr Gln Asp Pro Gly Pro Pro Pro Ser Pro Leu Leu Gly Leu	175	180	185		637
aag cca ttg cag ctg tta gaa gtg aaa gca agg gga aga ttt ggt tgt Lys Pro Leu Gln Leu Leu Glu Val Lys Ala Arg Gly Arg Phe Gly Cys	190	195	200	205	685
gtc tgg aaa gcc cag ttg ctc aat gaa tat gtg gct gtc aaa ata ttt Val Trp Lys Ala Gln Leu Leu Asn Glu Tyr Val Ala Val Lys Ile Phe	210	215	220		733
cca ata cag gac aaa cag tcc tgg cag aat gaa tat gaa gtc tat agt Pro Ile Gln Asp Lys Gln Ser Trp Gln Asn Glu Tyr Glu Val Tyr Ser	225	230	235		781

ctt ccc gtt atg aag cat gag aac ata cta cag ttc att ggt gca gag Leu Pro Gly Met Lys His Glu Asn Ile Leu Gln Phe Ile Gly Ala Glu 240 245 250	829
aaa aga ggc acc agt gtg gat gtg gac ctg tgg cta atc aca gca ttt Lys Arg Gly Thr Ser Val Asp Val Asp Leu Trp Leu Ile Thr Ala Phe 255 260 265	877
cat gaa aag ggc tca ctg tca gac ttt ctt aag gct aat gtg gtc tct His Glu Lys Gly Ser Leu Ser Asp Phe Leu Lys Ala Asn Val Val Ser 270 275 280 285	925
tgg aat car ctt tgt cat att gca gaa acc atg gct aga gga ttg gca Trp Asn Gln Leu Cys His Ile Ala Glu Thr Met Ala Arg Gly Leu Ala 290 295 300	973
tat tta cat gag gat ata cct ggc tta aaa gat ggc cac aag cct gca Tyr Leu His Glu Asp Ile Pro Gly Leu Lys Asp Gly His Lys Pro Ala 305 310 315	1021
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ctg aca gct tgc att gct gac ttt ggg ttg gcc tta aag ttc gag gct Leu Thr Ala Cys Ile Ala Asp Phe Gly Leu Ala Leu Lys Phe Glu Ala 335 340 345	1117
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gct tct cgt tgc act gct gca gat gga ccc gta gat gag tac atg tta Ala Ser Arg Cys Thr Ala Ala Asp Gly Pro Val Asp Glu Tyr Met Leu 400 405 410	1309
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gaa gtt gtt gtg cat aaa aaa aag agg cct gtt tta aga gat tat tgg Glu Val Val Val His Lys Lys Arg Pro Val Leu Arg Asp Tyr Trp 430 435 440 445	1405
cag aaa cat gca gga atg gca atg ctc tgt gaa acg ata gaa gaa tgt Gln Lys His Ala Gly Met Ala Met Leu Cys Glu Thr Ile Glu Glu Cys 450 455 460	1453

tgg gat cat gat gca gaa gcc agg tta tca gct gga tgt gta ggt gaa 1501
Trp Asp His Asp Ala Glu Ala Arg Leu Ser Ala Gly Cys Val Gly Glu
465 470 475

aga att act cag atg caa aga cta aca aat atc att act aca gag gac 1549
Arg Ile Thr Gln Met Gln Arg Leu Thr Asn Ile Ile Thr Thr Glu Asp
480 485 490

att gta aca gtg gtc aca atg gtg aca aat gtt gac ttt cct ccc aaa 1597
Ile Val Thr Val Val Thr Met Val Thr Asn Val Asp Phe Pro Pro Lys
495 500 505

gaa tct agt cta tgatggtggc accgtctgta cacactgagg actgggactc 1649
Glu Ser Ser Leu
510

tgaactggag ctgctaagct aaggaaaagtg cttagttgat tttctgtgtg aaatgagtag 1709

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ctgcaaactg taaagaacctt ctgaaaatgt actcgaagaa tgtggccctc tccaaatcaa 1889

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aatatgggt caccctaccc cccatactta tatcaaggc tcaaaaatatt cttttccatt 2489

tcaaagacag cactttgaaa accctaaatt acaagccagt agaagaaaaag ctaaaacacg 2549

ctttacaaat agcc 2563

<210> 16
<211> 513
<212> PRT
<213> Homo sapiens

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 20 25 30
 Phe Asn Ala Asn Trp Glu Lys Asp Arg Thr Asn Gln Thr Gly Val Glu
 35 40 45
 Pro Cys Tyr Gly Asp Lys Asp Lys Arg Arg His Cys Phe Ala Thr Trp
 50 55 60
 Lys Asn Ile Ser Gly Ser Ile Glu Ile Val Lys Gln Gly Cys Trp Leu
 65 70 75 80
 Asp Asp Ile Asn Cys Tyr Asp Arg Thr Asp Cys Val Glu Lys Lys Asp
 85 90 95
 Ser Pro Glu Val Tyr Phe Cys Cys Glu Gly Asn Met Cys Asn Glu
 100 105 110
 Lys Phe Ser Tyr Phe Pro Glu Met Glu Val Thr Gln Pro Thr Ser Asn
 115 120 125
 Pro Val Thr Pro Lys Pro Pro Tyr Tyr Asn Ile Leu Leu Tyr Ser Leu
 130 135 140
 Val Pro Leu Met Leu Ile Ala Gly Ile Val Ile Cys Ala Phe Trp Val
 145 150 155 160
 Tyr Arg His His Lys Met Ala Tyr Pro Pro Val Leu Val Pro Thr Gln
 165 170 175
 Asp Pro Gly Pro Pro Pro Ser Pro Leu Leu Gly Leu Lys Pro Leu
 180 185 190
 Gln Leu Leu Glu Val Lys Ala Arg Gly Arg Phe Gly Cys Val Trp Lys
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 Ala Gln Leu Leu Asn Glu Tyr Val Ala Val Lys Ile Phe Pro Ile Gln
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 Asp Lys Gln Ser Trp Gln Asn Glu Tyr Glu Val Tyr Ser Leu Pro Gly
 225 230 235 240
 Met Lys His Glu Asn Ile Leu Gln Phe Ile Gly Ala Glu Lys Arg Gly
 245 250 255
 Thr Ser Val Asp Val Asp Leu Trp Leu Ile Thr Ala Phe His Glu Lys
 260 265 270
 Gly Ser Leu Ser Asp Phe Leu Lys Ala Asn Val Val Ser Trp Asn Gln
 275 280 285
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 290 295 300
 Glu Asp Ile Pro Gly Leu Lys Asp Gly His Lys Pro Ala Ile Ser His
 305 310 315 320

Arg Asp Ile Lys Ser Lys Asn Val Leu Leu Lys Asn Asn Leu Thr Ala
325 330 335

Cys Ile Ala Asp Phe Gly Leu Ala Leu Lys Phe Glu Ala Gly Lys Ser
340 345 350

Ala Gly Asp Thr His Gly Gln Val Gly Thr Arg Arg Tyr Met Ala Pro
355 360 365

Glu Val Leu Glu Gly Ala Ile Asn Phe Gln Arg Asp Ala Phe Leu Arg
370 375 380

Ile Asp Met Tyr Ala Met Gly Leu Val Leu Trp Glu Leu Ala Ser Arg
385 390 395 400

Cys Thr Ala Ala Asp Gly Pro Val Asp Glu Tyr Met Leu Pro Phe Glu
405 410 415

Glu Glu Ile Gly Gln His Pro Ser Leu Glu Asp Met Gln Glu Val Val
420 425 430

Val His Lys Lys Arg Pro Val Leu Arg Asp Tyr Trp Gln Lys His
435 440 445

Ala Gly Met Ala Met Leu Cys Glu Thr Ile Glu Glu Cys Trp Asp His
450 455 460

Asp Ala Glu Ala Arg Leu Ser Ala Gly Cys Val Gly Glu Arg Ile Thr
465 470 475 480

Gln Met Gln Arg Leu Thr Asn Ile Ile Thr Thr Glu Asp Ile Val Thr
485 490 495

Val Val Thr Met Val Thr Asn Val Asp Phe Pro Pro Lys Glu Ser Ser
500 505 510

Leu